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NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months.

Bibliographic Source(s)

Subcommittee on Urinary Tract Infection, Steering Committee on Quality. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011 Sep;128(3):595-610. [61 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: American Academy of Pediatrics (AAP). The diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. Pediatrics 1999 Apr;103(4 Pt 1):843-52.

All clinical practice guidelines from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

Recommendations

Major Recommendations

Definitions for the quality of the evidence (A-D, X) and the strength of the recommendation (strong recommendation, recommendation, option) are provided at the end of the "Major Recommendations" field.

Diagnosis

Action Statement 1

If a clinician decides that a febrile infant with no apparent source for the fever requires antimicrobial therapy to be administered because of ill appearance or another pressing reason, the clinician should ensure that a urine specimen is obtained for both culture and urinalysis before an antimicrobial agent is administered; the specimen needs to be obtained through catheterization or suprapubic aspiration (SPA), because the diagnosis of urinary tract infection (UTI) cannot be established reliably through culture of urine collected in a bag (evidence quality: A; strong recommendation).

Action Statement 2

If a clinician assesses a febrile infant with no apparent source for the fever as not being so ill as to require immediate antimicrobial therapy, then the

clinician should assess the likelihood of UTI (see below for how to assess likelihood).

Action Statement 2a

If the clinician determines the febrile infant to have a low likelihood of UTI (see the text in the original guideline document), then clinical follow-up monitoring without testing is sufficient (evidence quality: A; strong recommendation).

Action Statement 2b

If the clinician determines that the febrile infant is not in a low-risk group (see below), then there are 2 choices (evidence quality: A; strong recommendation). Option 1 is to obtain a urine specimen through catheterization or SPA for culture and urinalysis. Option 2 is to obtain a urine specimen through the most convenient means and to perform a urinalysis. If the urinalysis results suggest a UTI (positive leukocyte esterase test results or nitrite test or microscopic analysis results positive for leukocytes or bacteria), then a urine specimen should be obtained through catheterization or SPA and cultured; if urinalysis of fresh (<1 hour since void) urine yields negative leukocyte esterase and nitrite test results, then it is reasonable to monitor the clinical course without initiating antimicrobial therapy, recognizing that negative urinalysis results do not rule out a UTI with certainty.

Action Statement 3

To establish the diagnosis of UTI, clinicians should require *both* urinalysis results that suggest infection (pyuria and/or bacteriuria) *and* the presence of at least 50,000 colony-forming units (CFUs) per mL of a uropathogen cultured from a urine specimen obtained through catheterization or SPA (evidence quality: C; recommendation).

Management

Action Statement 4

Action Statement 4a

When initiating treatment, the clinician should base the choice of route of administration on practical considerations. Initiating treatment orally or parenterally is equally efficacious. The clinician should base the choice of agent on local antimicrobial sensitivity patterns (if available) and should adjust the choice according to sensitivity testing of the isolated uropathogen (evidence quality: A; strong recommendation).

Action Statement 4b

The clinician should choose 7 to 14 days as the duration of antimicrobial therapy (evidence quality: B; recommendation).

Action Statement 5

Febrile infants with UTIs should undergo renal and bladder ultrasonography (RBUS) (evidence quality: C; recommendation).

Action Statement 6

Action Statement 6a

Voiding cystourethrography (VCUG) should not be performed routinely after the first febrile UTI; VCUG is indicated if RBUS reveals hydronephrosis, scarring, or other findings that would suggest either high-grade vesicoureteral reflux (VUR) or obstructive uropathy, as well as in other atypical or complex clinical circumstances (evidence quality B; recommendation).

Action Statement 6b

Further evaluation should be conducted if there is a recurrence of febrile UTI (evidence quality: X; recommendation).

Action Statement 7

After confirmation of UTI, the clinician should instruct parents or guardians to seek prompt medical evaluation (ideally within 48 hours) for future febrile illnesses, to ensure that recurrent infections can be detected and treated promptly (evidence quality: C; recommendation).

Definitions:

Strength of the Recommendations

Refer to Figure 1 in the guideline document for the definition of recommendation grades.

Evidence Quality

A	Well-designed randomized controlled trials (RCTs) or diagnostic studies on relevant population
B	RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, reasoning from first principles
X	Exceptional situations where validating studies cannot be performed and there is a clear preponderance of benefit or harm

Clinical Algorithm(s)

A clinical practice guideline algorithm is provided in the original guideline document.

Scope

Disease/Condition(s)

Urinary tract infection (UTI)

Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

Clinical Specialty

Emergency Medicine

Family Practice

Pediatrics

Intended Users

Hospitals

Physicians

Guideline Objective(s)

- To formulate recommendations for health care professionals about the diagnosis, treatment, and evaluation of an initial urinary tract infection (UTI) in febrile infants and young children (ages 2-24 months)
- To revise the American Academy of Pediatrics practice parameter regarding the diagnosis and management of initial UTIs in febrile infants

and young children

Target Population

Febrile infants and young children (2–24 months of age) who have no obvious neurologic or anatomic abnormalities known to be associated with recurrent urinary tract infection or renal damage

Interventions and Practices Considered

Diagnosis

1. History and physical examination
2. Gender-specific risk assessment
3. Urine collection by catheterization or suprapubic aspiration
4. Urine culture
5. Urinalysis (leukocyte esterase test, nitrite test, microscopic examination for white blood cells [WBCs] and bacteria)

Treatment/Management

1. Parenteral or oral antimicrobial regimens
2. Duration of treatment
3. Renal and bladder ultrasonography (RBUS)
4. Voiding cystourethrography (VCUG) as indicated
5. Advise parents/guardians to seek prompt medical evaluation for future febrile illnesses

Note: Antimicrobial prophylaxis and nuclear technetium-labeled dimercaptosuccinic acid scanning were considered but not recommended.

Major Outcomes Considered

- Sensitivity and specificity of diagnostic methods
- Rate of complications of recurrent infection, including progressive renal scarring
- Effectiveness of antimicrobial agent therapy

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Surveillance of Recent Literature

The authors searched Medline for articles published in the past 10 years with the medical subject headings "urinary tract infection" and "child (all)." The original search was conducted in 2007, but searches were repeated at intervals (approximately every 3 months) to identify new reports as the guideline was being developed. Titles were reviewed by 2 authors to identify all articles that were potentially relevant and seemed to contain original data. All titles that were considered potentially relevant by either reviewer were retained. Abstracts of selected articles were reviewed, again to identify articles that were relevant to the guideline and that seemed to contain original data. Review articles that were relevant also were retained for review. Again, all abstracts that were considered potentially relevant by either reviewer were retained. In addition, members of the

subcommittee submitted articles that they thought were relevant to be included in the review.

Selected articles were reviewed and summarized by 2 reviewers. The summaries were reviewed, and articles presenting potentially new information were retained. In addition, representative articles reinforcing evidence in the 1999 technical report were retained.

Targeted Literature Search and Meta-analysis

To examine specifically the effectiveness of antimicrobial prophylaxis to prevent recurrent urinary tract infection (UTI) and pyelonephritis in children with vesicoureteral reflux (VUR), a formal meta-analysis of randomized controlled trials (RCTs) was conducted. First, a systematic literature review focused on RCTs, including studies in press, was performed.

Inclusion Criteria

RCTs published in the past 15 years (1993–2009) that compared antimicrobial treatment versus no treatment or placebo treatment for the prevention of recurrent UTI and included a minimum of 6 months of follow-up monitoring were included. Published articles, articles in press, and published abstracts were included. There were no language restrictions. To be included, studies needed to enroll children who had undergone voiding cystourethrography (VCUG) for determination of the presence and grade of VUR. Studies that examined antibiotic prophylaxis versus no treatment or placebo treatment were included.

Search Methods

The initial literature search was conducted on June 24, 2008, and the search was repeated on April 14, 2009. Studies were obtained from the following databases: Medline (1993 to June 2008), Embase (1993 to June 2008), Cochrane Central Register for Controlled Trials, bibliographies of identified relevant articles and reviews, and the Web site www.ClinicalTrials.gov. See the Technical Report for the list of search terms (see the "Companion Documents" field).

The search strategy and the screening of the titles for selection of potentially relevant abstracts were completed by 1 reviewer. Two reviewers screened selected abstracts to identify appropriate articles. Published articles and abstracts that met the inclusion criteria were included in the meta-analysis. Additional information was sought from authors whose articles or abstracts did not contain the information needed for a decision regarding inclusion. The selection process is summarized in Figure 2 of the Technical Report (see the "Companion Documents" field).

Number of Source Documents

The surveillance of recent literature yielded 1308 titles. Of those, 297 abstracts were selected for review. From among the abstracts, 159 articles were selected for full review.

Meta-analysis

45 titles were selected for abstract review. 7 abstracts were selected for full review, plus 2 highly relevant articles published after the literature search. 8 articles were included for meta-analyses.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Quality

A	Well-designed randomized controlled trials (RCTs) or diagnostic studies on relevant population
B	RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)

D	Expert opinion, case reports, reasoning from first principles
X	Exceptional situations where validating studies cannot be performed and there is a clear preponderance of benefit or harm

Methods Used to Analyze the Evidence

Meta-Analysis of Individual Patient Data

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Original Guideline Data Analysis

Data from 402 articles were extracted and recorded in evidence tables, using an Excel (Microsoft Corporation, Redmond, WA) spreadsheet. A subset of 24 articles was reviewed twice by different reviewers to check interrater reliability. At the time of analysis of the decision models, the articles were reviewed again by the epidemiology consultant.

A conceptual evidence model of the diagnosis and management of urinary tract infection (UTI) was used to generate a decision tree. The comprehensive literature review determined the probability estimates used in the tree. The tree was then used to conduct risk analyses and cost-effectiveness analyses of alternative strategies for the diagnosis and management of UTI. Based on the results of these analyses and consensus when necessary, an algorithm representing the strategies with acceptable risk-benefit trade-offs was developed.

Updated Analysis

Assessment of Studies

The quality of selected articles and abstracts was assessed with the scoring system described by Downs and Black in 1998. Each study received scores (from 2 assessors) on a scale from 0 to 32. Six of the articles and abstracts were included in a first meta-analysis, which evaluated febrile UTI or pyelonephritis as the outcome. A second meta-analysis, which included all studies with the outcome "all UTI," also was conducted.

Meta-analyses

All statistical tests were performed by using Review Manager 5.1 (Nordic Cochrane Centre, Copenhagen, Denmark). The following settings were used for the analyses: dichotomous outcome and Mantel-Haenzel statistical method. Data were analyzed with a random-effects model. When no statistically significant effect and no statistical heterogeneity were detected, data also were analyzed with a fixed-effects model, because that type of analysis is more likely to detect a difference. The effect measure was presented as a risk ratio (RR). The results for the primary outcome (pyelonephritis or febrile UTI) and the secondary outcome (any type of UTI, including cystitis, nonfebrile UTI, and asymptomatic bacteriuria) were calculated as point estimates with corresponding 95% confidence intervals (CIs). Heterogeneity was analyzed by using the Q statistic with a threshold of $P<.05$. The number of studies was insufficient for assessment of publication bias with a funnel plot.

Meta-analyses of Data According to Vesicoureteral Reflux (VUR) Grade and for Children 2 to 24 Months of Age

The published data on which the meta-analyses were based did not contain subgroup data relevant to the practice guideline. Specifically, some studies did not report outcomes according to the severity of VUR, and some did not report outcomes specific to the age range of interest (2–24 months). Therefore, the committee chairperson contacted the authors of the reports included in the meta-analysis, to obtain original data. Data on recurrence according to VUR grade and for the subgroup of children 2 to 24 months of age were received from the authors, and these data were analyzed in separate meta-analyses.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Results from the literature searches and meta-analyses were provided to committee members. Issues were raised and discussed until consensus was reached regarding recommendations. The quality of evidence supporting each recommendation and the strength of the recommendation were

assessed by the committee member most experienced in informatics and epidemiology and were graded according to American Academy of Pediatrics (AAP) policy (see Figure 1 in the guideline document).

Rating Scheme for the Strength of the Recommendations

Strength of the Recommendations

Refer to Figure 1 in the guideline document for the definition of recommendation grades.

Cost Analysis

The cost-effectiveness analysis in the accompanying technical report was used to quantify the trade-offs between cost and clinical effect when moving from one clinical strategy to another.

- The cost-effectiveness analysis using the data for the original guideline led to the conclusion that diagnosis and treatment of urinary tract infection (UTI) and evaluation for urinary tract anomalies had borderline cost-effectiveness, costing approximately $700,000 per case of hypertension or end-stage renal disease prevented.
- The technical report for the 1999 guideline examined the effects of age, gender, and circumcision status on the prevalence of UTI. The conclusion was that boys more than 1 year of age who had been circumcised were at sufficiently low risk of UTI (<1%) that evaluation of this subpopulation would not be cost-effective. New work confirms an approximately threefold to fourfold decreased risk of UTI among circumcised boys. The difference seems to be greater for younger children.
- In light of the marginal cost-effectiveness of the procedure found under the more-optimistic assumptions in the 1999 technical report, the data argue against voiding cystourethrography (VCUG) after the first UTI.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was reviewed by multiple groups within the American Academy of Pediatrics (7 committees, 1 council, and 9 sections) and 5 external organizations in the United States and Canada.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is provided for each recommendation (see the "Major Recommendations" field).

The recommendations were based on an updated literature search and meta-analyses of primary data.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Timely, appropriate, and effective diagnosis of urinary tract infection (UTI) in febrile infants and children aged 0-24 months
- Timely and appropriate treatment of UTI to prevent the spread of infection and renal scarring
- Avoidance of overdiagnosis of UTI, which can prevent overtreatment, unnecessary and expensive imaging, and unnecessary radiation

exposure

Potential Harms

- Suprapubic aspiration (SPA) has limited risks, but technical expertise and experience are required, and many parents and physicians perceive the procedure as unacceptably invasive, compared with catheterization. However, there may be no acceptable alternative to SPA for boys with moderate or severe phimosis or girls with tight labial adhesions.
- Catheterization is invasive and may be painful.
- A small proportion of febrile infants, considered at low likelihood of UTI, will not receive timely identification and treatment of their UTIs.
- Stringent diagnostic criteria of urine cultures may miss a small number of UTIs.
- Treatment of asymptomatic bacteriuria may be harmful.
- Between 2% and 3% of imaging examinations will be false-positive results, leading to unnecessary and invasive evaluations.
- Based on the recommendations, detection of a small number of cases of high-grade reflux and correctable abnormalities using voiding cystourethrography is delayed. However, the risks associated with radiation (plus the expense and discomfort of the procedure) for the vast majority of infants outweigh the risk of delaying the detection of the few with correctable abnormalities until their second UTI.
- Voiding cystourethrography (VCUG) is an uncomfortable, costly procedure that involves radiation, including to the ovaries of girls.
- There may be additional costs and inconvenience to parents with more-frequent visits to the clinician for evaluation of additional febrile illnesses.
- Incubation time, which is inherent in the culture process, results in delayed treatment or presumptive treatment on the basis of tests that lack the desired sensitivity and specificity to replace culture.
- Barriers to the effectiveness of antimicrobial prophylaxis are adherence to a daily regimen, adverse effects associated with the various agents, and the potential for emergence of antimicrobial resistance.

Qualifying Statements

Qualifying Statements

- This clinical practice guideline is not intended to be a sole source of guidance for the treatment of febrile infants with urinary tract infections (UTIs). Rather, it is intended to assist clinicians in decision-making. It is not intended to replace clinical judgment or to establish an exclusive protocol for the care of all children with this condition.
- The recommendations in this report do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.
- The basis of the determination that antimicrobial therapy is needed urgently is not specified, because variability in clinical judgment is expected; considerations for individual patients, such as availability of follow-up care, may enter into the decision, and the literature provides only general guidance.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Subcommittee on Urinary Tract Infection, Steering Committee on Quality. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011 Sep;128(3):595-610. [61 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1995 Apr 5 (revised 2011 Sep)

Guideline Developer(s)

American Academy of Pediatrics - Medical Specialty Society

Source(s) of Funding

The American Academy of Pediatrics has neither solicited nor accepted any commercial involvement in the development of the content of this publication.

Guideline Committee

Steering Committee on Quality Improvement and Management; Subcommittee on Urinary Tract Infection

Composition of Group That Authored the Guideline

The subcommittee was composed of pediatricians with expertise in the fields of epidemiology and informatics, infectious diseases, nephrology, pediatric practice, radiology, and urology.

Subcommittee on Urinary Tract Infection, 2009-2011: Kenneth B. Roberts, MD (*Chair*); Stephen M. Downs, MD, MS; S. Maria E. Finnell,

MD, MS; Stanley Hellerstein, MD; Linda D. Shortliffe, MD; Ellen R. Wald, MD; J. Michael Zerin, MD

Financial Disclosures/Conflicts of Interest

All authors have filed conflict of interest statements with the American Academy of Pediatrics. Any conflicts have been resolved through a process approved by the Board of Directors.

None of the participants had any financial conflicts of interest.

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Guideline Availability

Electronic copies: Available from the American Academy of Pediatrics (AAP) Policy Web site .

Print copies: Available from AAP, 141 Northwest Point Blvd., P.O. Box 927, Elk Grove Village, IL 60009-0927.

Availability of Companion Documents

The following is available:

- Technical report: urinary tract infections in febrile infants and young children. Pediatrics 2011 Sep Apr;128(3):e749-e770. Electronic copies: Available from the American Academy of Pediatrics (AAP) Policy Web site .

Print copies: Available from AAP, 141 Northwest Point Blvd., P.O. Box 927, Elk Grove Village, IL 60009-0927.

Patient Resources

None available

NGC Status

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